



Research Article

Ruptured Intracranial Aneurysms Operated in Antananarivo: Epidemiology and Prognosis Factors

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Abstract

Introduction: Ruptured intracranial aneurysm is a diagnostic and therapeutic emergency. Surgery remains the only therapeutic option available in Madagascar.

Method: This is a retrospective, descriptive and analytical, multicenter study over a period of 4 years (January 2017 to December 2020) in the Neurosurgery Department of the public hospital in Antananarivo. The objective of this study is to determine the epidemic-clinical profile and prognostic factor of ruptured and operated intracranial aneurysm. The regression coefficient or estimation that quantifies the association between the variables was performed, considering a statistical significance threshold of $p < 0.05$

Results: 55 patients were included, 19 men and 36 women, aged 30 to 72 years with a mean age of 50 years. The most reported medical history was hypertension (60%), alcoholism (42%), and smoking (33%). The majority of patients (71%) consulted within the first 3 days after the onset of symptoms, for sudden headaches (62%) or consciousness disorders (36%). The clinical examination revealed a Glasgow score of 15 (42%) and 14 (18%). The Hunt and Hess score and the WFNS score were 2 in 44% and 40% of cases respectively. On the brain scan, the Fischer score was 3 in 40% of cases and the aneurysm was in the anterior communicating artery in 45% of cases. None of the patients could benefit from cerebral arteriography due to the unavailability of the latter in the country. Surgery was performed after the 10th day in 34% of cases, and the outcome was favorable in 65% of cases. A mortality rate of 22% was observed. Among the prognostic factors associated with death; we note: Glasgow score less than or equal to 7 ($p = 0.0001$) and Fischer score greater than or equal to 3 ($p = 0.009$).

Conclusion: The epidemiological profile of ruptured intracranial aneurysms in our context is superimposable to that of the literature. Access to modern neuroradiology remains limited and underestimates their incidence. Surgical securing of the aneurysm offers a better result despite the rather high death rate.

Keywords: Epidemiology; Intracranial Aneurysm; Mortality; Prognosis; Surgery

Introduction

Intracranial Arterial Aneurysms (IAA) are vascular malformations characterized by a localized dilatation of the arterial wall, secondary to a thinning of the media by a loss of the internal elastic boundary [1]. Rupture is the main mode of discovery of intracranial aneurysms, leading to Subarachnoid Hemorrhage (SAH) or meningeal hemorrhage, sometimes associated with an intracerebral hematoma and/or intraventricular hemorrhage. It is a major diagnostic and therapeutic emergency that requires a multidisciplinary and specialized management, whose etiological treatment consists of exclusion by surgical clipping of the aneurysm, or by endovascular embolization.

The mortality rate of ruptured aneurysms is very high, up to 50% in the absence of management [2]. Currently, the improvement of diagnostic and therapeutic resources tends to decrease this rate significantly. One year mortality was reduced to 23.7% after coiling and to 30.6% after clipping [3]. Only surgical exclusion of the aneurysm is available in Madagascar among the recommended etiological therapeutic options. This is the first multicenter study of intracranial aneurysms in Madagascar. The aim of this study is to establish their epidemiological profile, to evaluate the results of their surgical management and finally to determine the prognostic factors associated with death.

Method

This is a retrospective, descriptive, analytical study of cases of ruptured intracranial aneurysms operated on in the three neurosurgery departments in Antananarivo Madagascar. It was carried out over a period of 4 years, from 01 January 2017 to 31 December 2020. The services concerned are: the Neurosurgery Department of the Joseph Ravoahangy Andrianavalona University Hospital (CHU-JRA), the Soavinadriana Hospital (CENHNSOA) and the Anosiala University Hospital. The records of hospitalized patients with subarachnoid hemorrhage due to aneurysm rupture confirmed by cerebral angioscan and who underwent surgical clipping were included. The data were collected by consulting the registers of each neurosurgical department concerned, then the files of the patients meeting our inclusion criteria. Several parameters were studied such as:

- Epidemiological variables including gender, age, lifestyle (smoking, alcoholism) and medical history (arterial hypertension)
- Clinical variables including time to medical consultation (time interval between onset of symptoms and time of consultation), reason for consultation, initial Glasgow score, Hunt and Hess score (Appendix 1) [4], and World Federation of Neurological

Surgeons (WFNS) score at admission (Appendix 2) [5],

- The scans of the subarachnoid hemorrhage including the Fischer score (Appendix 3) [6] and the aneurysmal location,
- Arteriography was not performed due to the unavailability of this technique in Madagascar
- The time between the diagnosis and the realization of the surgical intervention
- The evolution after the treatments. The analytical study of the data was carried out using the SPSS 20 statistical software. The regression or estimation coefficient that quantifies the link between the variables was carried out, considering a threshold of statistical significance of $p < 0.05$.

Results

Epidemiological Parameters

- Frequency:** A total of 55 cases were selected. Twenty-five cases (45%) were operated on at the CHUJRA, 22 (40% of cases) at the CENHNSOA and 8 (15% of cases) at the CHU of Anosiala.
- Age and gender:** The median age of the patients was 50 years, ranging from 30 to 72 years, of which 19 patients (34% of the cases) were in their 40s and 16 patients (29% of the cases) were in their 50s. Among these patients, we counted 36 women (65%) and 19 men (35%) with a male/female ratio of 1/1.9 (sex ratio: 0.53).
- History:** Among the toxic habits and medical history of the patients, we observed 33 hypertensive patients (60% of the cases), 23 chronic ethylic patients (41% of the cases) and 18 smoking patients (33% of the cases).

Clinical Parameters

- Time and reasons for consultation:** Patients arrived in the emergency room around the second and third day after the onset of symptoms in 20% of cases (11 patients). Only 18% of the cases (10 patients) consulted the same day as the onset of symptoms. Among the symptoms found at the consultation, brutal headaches were reported by 34 patients (62% of cases), followed by consciousness disorders in 20 patients (36%), vomiting in 15 patients (27%), seizures in 7 patients (13%) and agitation in 2 patients (4%).
- Initial Glasgow score:** Patients had a GCS score of 15 in 42% of cases (23 patients) during the initial clinical evaluation. Only 10 patients (18% of cases) were comatose, with a GCS score less than or equal to 7 at initial management.
- Initial Hunt and Hess score:** On initial clinical examination, 24 patients (44% of cases) had a Hunt and Hess score of II, 12 patients (22%) of III, 9 patients (16%) of V, 6 patients (11%)

of IV, and 4 patients (7%) had a score of I.

- iv. **WFNS score at admission:** The WFNS score at II was most frequently observed (in 22 patients, or 40%); 11 patients (20%) had a score at I, 10 patients (18%) at IV, 6 patients (11%) at III, and another 6 patients (11%) with a score at V.

Paraclinical Examinations

All patients had a cerebral CT scan without contrast injection and a cerebral angioscan after hospital admission. The subarachnoid hemorrhage was classified according to the Fischer score and the location of the ruptured aneurysm was identified on the cerebral angioscan.

- i. **Fischer score:** Subarachnoid hemorrhage and possible associated intra-parenchymal or intra-ventricular hemorrhage were identified on brain CT without contrast injection. Twenty-two patients (i.e., 40% of the cases) were classified as Fischer III, 17 patients as Fischer II (i.e., 31% of the cases) and 16 patients (i.e., 29% of the cases) as Fischer IV.
- ii. **Location of the aneurysm:** The aneurysm was in the anterior circulation in the majority of cases. It was in the anterior communicating artery in 45% of the cases (25 patients), in the middle cerebral artery or sylvian artery in 35% of the cases (19 patients), in the internal carotid artery in 9% (5 cases). A posterior cerebral artery aneurysm and a carotid-ophthalmic aneurysm were observed in 2 cases each (4%). An anterior cerebral artery aneurysm was present in 1 case. Only one

case of aneurysm (2% of cases) was observed in the posterior circulation, specifically in the posteroinferior cerebellar artery.

Surgical Parameters

All patients had undergone aneurysmal securing by surgical clipping.

- i. **Time to surgical management:** Surgery was performed after the tenth day in 19 patients (34% of the cases), then on the second day in 9 patients (16% of the cases), and on the third and fifth days after admission in 6 patients (11% of the cases) of each.
- ii. **Post-operative follow-up of patients:** The evolution was favorable in 65% of the cases (36 patients). We observed 22% of cases of death (i.e., 12 patients) after the surgical management and 13% of cases (i.e. 7 patients) of complications marked by the appearance or aggravation of consciousness disorders, neurological deficits ranging from hemiparesis to hemiplegia, simple or associated with aphasia.
- iii. **Evaluation of factors associated with death:** Several factors suspected of being related to death in patients with ruptured AIC were evaluated in our study. Among these factors, we list gender, age, initial GCS score, Fischer score, location of the ruptured AIC, and time to surgical management beyond 10 days. A significant association was found for GCS score less than or equal to 7 with a p-value of 0.0001 and Fischer subarachnoid hemorrhage greater than or equal to 3 with a p-value of 0.009 (Table 1).

Risk factors	Total n (%)	Deceased n (%)	Non-deceased n (%)	P-value
Female gender	36 (66%)	7 (58%)	29 (64%)	0,557
Age greater than to 50 years	28 (51%)	8 (67%)	20 (47%)	0,217
Initial GCS less than or equal to 7	10 (18%)	9 (75%)	1 (23%)	0,0001
Fischer score greater than or equal to 3	38 (69%)	12 (100%)	26 (61%)	0,009
Anterior communicant	25 (46%)	8 (67%)	17 (40%)	0,095
Time to surgery less than to 10 days	19 (35%)	2 (29%)	17 (35%)	0,722

Table 1: Evaluation of factors associated with mortality in ruptured ACL surgery.

Discussion

Epidemiological Parameters

I. Frequency: The incidence of intracranial aneurysm varies widely in the literature and by country. In Japan in 2007, Rooij et al [7] found a high incidence, reaching 22.7/100,000 inhabitants/year. In our study, there were 55 cases of ruptured AIC operated for 4 years. This value does not reflect the real prevalence of ruptured ICA in the country. Indeed, several patients escape counting, because our study is limited to neurosurgical services. Moreover, in case of ruptured AIC, 10 to 15% of patients die before reaching the hospital [8].

II. Gender and age: Our study found a predominance of female patients with a sex ratio of 0.53. The meta-analysis of Locksley et al [9] on a large study population (6368 cases of subarachnoid hemorrhage due to aneurysmal rupture) allowed the realization of a curve of evolution of the sex ratio according to the age and highlighted the predominance of the male gender before the age of 40 years, and a predominance of the female gender after the age of 40 years. The female predominance from the age of 40 onwards can be explained by the greater life expectancy of women compared to men and by the decrease in the blood concentration of estrogen during and after the menopause. In fact, taking hormone replacement therapy during menopause is a protective factor for aneurysmal SAH [10].

III. Lifestyle and history: Over time, several risk factors for aneurysmal formation and rupture have been recognized in the literature. The most reported were hypertension, smoking and alcohol.

i. Arterial hypertension: In our study, hypertension was observed in 60% of cases. Taylor et al [11], in their study of 20,767 unruptured ICAs hospitalized in Medicare, observed that arterial hypertension was a significant risk factor for SAH with an RR=1.46 (95% CI: 1.01-2.11). Wang Y et al [12] confirmed the causal role of systemic hypertension in the formation and rupture of intracranial aneurysms in their laboratory study in animal models. Although our study is not a case-control study, our result is in line with the literature on this risk factor.

ii. Smoking: Our study found 42% of smokers among aneurysmal meningeal hemorrhage. The prospective multicenter study of Weir et al [13], in a national American and European survey, found a 2.5-fold higher rate of smoking in patients with aneurysmal meningeal hemorrhage. Experimental laboratory data suggested a strong involvement of smoking in the induction of a vascular inflammation reaction, which would participate in the formation and rupture of cerebral aneurysms [14]. Our study agrees with the data in the literature on the

role of smoking in the etiopathogeny of aneurysmal SAH.

iii. Alcohol: Several lifestyle risk factors may influence, to varying degrees, the formation and rupture of intracranial aneurysms. In our study, 42% of the study population were alcoholics. In Finland, some investigators [15] have attributed the higher rate and reversal of the usual female-to-male ratio of aneurysmal SAH to excessive alcohol consumption by the population. Alcoholism would seem to play a role as a risk factor for the occurrence of aneurysmal SAH given the proportion of this factor in our population. Nevertheless, a higher level of evidence is needed to confirm this hypothesis.

Clinical Parameters

i. Time and reasons for Consultation: In our study, 71% of the patients had consulted within the first 3 days after the aneurysmal rupture and 16% of the cases after the 6th day. In Africa, several reasons explain the delay in consultation, such as the isolation of certain cities, the problem of transferring patients, diagnostic erraticism, the inaccessibility of the scanner, and the absence of social security and/or the lack of means. These delays in consultation would increase the mortality of ruptured AIC. Indeed, Greenberg et al [8] reported a mortality rate in the first days of aneurysmal rupture up to 10% of cases and a mortality after 30 days up to 46% of cases. Rupture is the most frequent circumstance of discovery of intracranial aneurysms. In our study, patients reported headache of sudden onset in 62% of cases, consciousness disturbances in 36% of cases and seizures in 13% of cases. According to Walls et al [16], headache is the main symptom and is described as a “thunderclap in a serene sky”. Thus, any patient presenting with a headache of sudden onset, rapid aggravation, and high intensity, should first evoke an aneurysmal SAH. However, the neurological examination may be normal in up to 50% of cases [17].

ii. Initial Glasgow score or Glasgow Coma Scale (GCS): The evaluation of the Glasgow score or the Glasgow Coma Scale (GCS) is an essential part of the clinical examination at admission. In our study, the majority of patients (60%) were conscious on admission with a GCS score of 15/15 in 42% of cases and 14/15 in 18% of cases. Eighteen percent (18%) of patients were comatose. Indeed, the Glasgow score was used to assess the depth of comas [18].

iii. Hunt and Hess score: Although it was criticized for mixing objective and subjective signs in its classification, the Hunt and Hess score [4] remained the most widely used in published scientific articles, employed by about 70% of authors according to Oshiro et al [19]. In our study, we had a predominance of grade II (44%) of the Hunt and Hess score, followed by grade III (22%), then grade V (16%), grade IV (11%) and grade I (7%). The study of Henkes et al [20] in Germany in 2003 had

noted a percentage inversely proportional to the grades of the Hunt and Hess score: grade I (26%) is followed by grade II (25.3%), then grade III (21.1%), grade IV (15.9%) and grade V (8%). The predominance of conscious patients (grade I and II) in our series could be related to the long delay in consultation of our study population. Indeed, the latter have a better survival rate than patients developing severe meningeal hemorrhage (grade IV and V).

iv. World Federation of Neurological Surgeons (WFNS) score: It was created to overcome the shortcomings of its predecessors by using objective criteria [5]. In our study, we found a grade II (40%) in the majority, followed by grade I (20%), then grade IV (18%) and finally grade III and V which each had 11%. The study of Ramnarayan et al [21] showed a predominance of grade I (63%), followed by grade II (17%), then grade III (10%), grade IV (6%) and finally grade V (4%). The study by Hayat et al [20] found grade I in 44% of cases, followed by grade III (31%), grade IV (15%) and grade II (10%). No grade V was observed. The data in the literature, including that of our study, had a clinical grade less than or equal to 3 majority, either in the WFNS or Hunt and Hess classification. According to Oshiro et al [19], the Glasgow Coma Scale (GCS) and its derivative, the WFNS scale (Appendix 2), would be the best scale for predicting functional prognosis.

Paraclinical Examinations

i. Cerebral CT scan without contrast injection and cerebral angioscan: The extent of subarachnoid hemorrhage is assessed according to the Fisher scale (Appendix 3), which also has a prognostic value correlated to the risk of vasospasm [6]. The majority of our patients had a Fisher grade III score (40%), followed by grade II (30.91%), then grade IV (29.09%) and no grade I found. Roethlisberger et al [22] observed a majority of grade III (53.4%), then grade IV (33.1%), grade II (10.6%) and finally grade I (2.9%). Our study population presents a grade of SAH corresponding to the data in the literature. Prescribed at the same time as the cerebral CT scan without injection of contrast medium, the cerebral angioscan can demonstrate aneurysms from 2 to 3 mm in diameter and can detect up to 97% of intracranial aneurysms, ruptured or not [23]. It is essential to identify the side, location, number, and size of the intracranial aneurysm. Other more efficient neuroradiological examinations, including Flair sequence MRI angiography to detect subacute meningeal hemorrhage and conventional cerebral angiography of diagnostic and therapeutic interest, are routine in developed countries. Cerebral angiography does not yet exist in Madagascar. Interventional radiography remains an area to be developed to improve the therapeutic outcome of ruptured AIC in Madagascar.

ii. Location of intracranial aneurysm: In our study, 95% of ruptured ICAs were located in the anterior circulation, mainly in the anterior communicating artery (45% of cases). Kotowski et al [24] in 2013 found 87% of ruptured ICAs in the anterior circulation and 13% in the posterior circulation. The study by Cesarini et al [25] in 1999 noted 37% aneurysms in the anterior communicating artery, 33% in the middle cerebral artery, and only 7% in the posterior circulation. Our result agrees with that of the literature which finds a predominance of aneurysmal localization in the anterior circulation of the polygon of Willis, with a majority in the anterior communicating artery, followed by the middle cerebral artery.

Surgical Parameters

Only surgical means are available in Madagascar to secure any type of AIC.

I. Timing of surgical aneurysmal clipping: The optimal timing of surgery still remains a controversial topic in the literature. Zhao et al [26] compared the results of early (less than to 72hours) and late (greater than to 72h) surgery in 118 patients; they found no significant difference in the number of days of hospitalization and outcome of the operated patients. In our study, 61% of the patients were operated on within the first week after their hospitalization, and 34% were operated on after the 10th day. Even if no precise consensus is found in the literature, Nieuwkamp et al [27] strongly recommended early management (within 72 hours after the meningeal hemorrhage) of ruptured AIC, because of the risk of rebleeding.

II. Surgical Outcome: The outcome of aneurysmal surgical exclusion in our study has 65% favorable outcome with or without minimal neurological sequelae (GOS 4 and 5), 13% major neurological sequelae and/or patients in vegetative state (GOS 3 and 2), and a postoperative mortality of 22%. Nieuwkamp [2] had described that the case fatality of aneurysmal subarachnoid hemorrhage in developed countries decreased by 17% during the period from 1973 to 2002, with regional differences. This decrease in case fatality was related to improvements in diagnostic and therapeutic strategies for ruptured aneurysms. In Madagascar, the mortality rate remains high compared with those in the literature, even in Africa. Some postoperative complications, notably arterial vasospasm, remain frequent and severe, requiring endovascular treatment, which is currently unavailable in Madagascar.

III. Factors Associated with Death: Among the mortality factors evaluated in our study, GCS score ≤ 7 and Fischer meningeal hemorrhage ≥ 3 were significantly associated with mortality in ruptured ICA surgery. No significant statistical associations were found for gender, age, and aneurysm location. Other mortality factors are strongly recognized in the literature [24],

such as the size of intracranial aneurysms, but which we could not evaluate due to lack of adequate data in our study related to the absence of angiography examination in our context (Gold standard of morphological evaluation of AIC).

- i. Initial GCS and death:** Our study found a significant association between patient mortality and initial GCS score less than or equal to 7 with a p-value at 0.0001. In the systematic review by Wartenberg et al [28], initial neurological status assessed by the Hunt and Hess score, was the most reported first predictor of mortality. GCS score less than or equal to 7 on patient admission determines WFNS grade 4 or 5, which in turn defines severe meningeal hemorrhage, with a median mortality rate of 27% in Japan, 32% in the United States, and 43% in Europe [28]. The GCS is the most reproducible and objective clinical severity scale and is present in the WFNS scale that some authors strongly recommend [5].
- ii. Fischer score and death:** Our study found a significant association between meningeal hemorrhage size and mortality, especially for Fischer score greater than or equal to 3 (p-value = 0.009). The volume of SAH on brain CT informs about the risk of vasospasm, which can lead to delayed cerebral ischemia and influence outcome [6]. Several reviews of the literature have evaluated this relationship and found a graded and proportional association between SAH thickness and disease outcome. Indeed, a significant association with death and major disability has been found [29] with an increased risk of vasospasm up to 20% for Fischer grades III and IV [30].
- iii. Age and death:** In our series, age greater than or equal to 50 years was not significantly associated (p-value = 0.217) with mortality of ICA surgery, as in the study of Kototowski [24] and Laidlaw [31] for patients older than 55 years (p-value = 0.18) and older than 70 years (p-value > 0.05) respectively. However, according to Wartenberg et al [28], age was the second most important predictor of intracranial aneurysm mortality, after the patient's initial clinical condition. Danish and Swedish studies [32] had shown that age alone is insufficient to increase the prognosis; however, the association with smoking and aneurysmal size would make this prognosis more severe. This can be explained by the effect of smoking on the vessels which are already fragile in the elderly subject.
- iv. Aneurysmal location and death:** In our series, we have a predominance of anterior aneurysmal localization (95%), particularly in the anterior communicating (45%). However, the latter was not significantly associated (p-value = 0.095) with mortality in ruptured ICA surgery. Indeed, the literature rather incriminates the location at the level of the posterior circulation. Wiebers et al [33] had found a poor outcome with a relative risk at 2.25 for the posterior circulation (99% CI: 1.1-4.4; p-value = 0.02), compared with 1.6 for the anterior

circulation (99% CI: 1.1-2.4; p-value less than or equal to 0.0001), at one year after aneurysmal securing, whatever the technique performed (embolization or surgical clipping). Kotowski et al [24] in 2012 had found a morbi-mortality of surgical treatment in the order of 5.7% (99% CI: 2.3-13.3) for anterior circulation and 15.6% (99% CI: 7.4-30.1) for posterior circulation, with a relative risk of 4.1 (95% CI: 2.3-7.6) for the latter. Indeed, surgery for aneurysms of the posterior circulation, particularly giant aneurysms of the basilar artery bifurcation, is technically more difficult with an increased surgical risk.

Conclusion

Meningeal hemorrhage due to aneurysmal rupture is a serious pathology, with a high morbidity and mortality rate despite appropriate management. It is a life-threatening emergency that should not suffer from any diagnostic and therapeutic delay. Our study concluded that the epidemiology of ruptured intracranial aneurysms is similar to the literature. The delay in consultation and surgical management has a negative impact on the results. The mortality rate is still high, and the prognostic factors are Glasgow score less than or equal to 7 and Fischer score greater than or equal to 3. Our study has some limitations, namely the number of samples which is quite representative, the difficulty of access to modern neuroimaging explorations, and even the absence of the latter. The technical difficulty of intracranial aneurysm surgery is mainly related to the lack of adequate operating equipment in some departments. Surgical securing of the aneurysm offers a better result for the complete exclusion of the malformation. Nevertheless, endovascular treatment reduces complications. Thus, the wishes to have this new modern technique on site are formulated.

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Appendixes

Grade	Description	Mortality
1	Asymptomatic or mild headache and neck stiffness	15%
2	Cranial nerve palsy (example III, IV), moderate to severe headache, stiff neck	30%
3	Moderate focal deficit, lethargy or confusion	50%
4	Stupor, moderate to severe hemiparesis, decortication rigidity	65%
5	Deep coma, rigidity of decerebration, apparent death	95%

Appendix 1: Hunt and Hess clinical classification of aneurysmal SAH [4].

Score WFNS	Score GCS	Major focal deficit (aphasia, hemiparesis or hemiplegia)
0	Intact aneurysm	
1	15	Absent
2	13 - 14	Absent
3	13 - 14	Present
4	7 - 12	Present or absent
5	3 - 6	Present or absent

Appendix 2: World Federation of Neurological Surgeons' scale for subarachnoid hemorrhage [5].

Score de Fischer	SAH on brain scan	Risk of vasospasm
0	No subarachnoid hemorrhage (SAH) or intraventricular hemorrhage (IVH)	
1	Fine focal or diffuse SAH, without HIV	24%
2	Fine focal or diffuse SAH with HIV	33%
3	Thick focal or diffuse SAH, without HIV	33%
4	Thick focal or diffuse SAH, with HIV	40%

Appendix 3: Modified Fischer score and risk of vasospasm [6].